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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Hiroyuki Kamiya

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EXAMINER

PANDE, SUCHIRA

ART UNIT

PAPER NUMBER

1637

MAIL DATE

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/588,792	<b>Applicant(s)</b> KAMIYA ET AL.	
	<b>Examiner</b> SUCHIRA PANDE	<b>Art Unit</b> 1637	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 02 September 2009.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 12-22 is/are pending in the application.
- 4a) Of the above claim(s) 17-22 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 12-16 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Claim Status***

1. Amendment filed on September 2, 2009 is acknowledged. Applicant has cancelled claims 1-11; amended base claim 1; withdrawn claims 17-22. Claims 12-16 are currently active and will be examined in this action.

### ***Response to Arguments***

#### Re 103 rejection of claims 12-16 over Moriya and Zarling et al.

2. Applicant's arguments filed 9/2/09 have been fully considered but they are not persuasive. Applicant correctly argues that Zarling et al. does not refer to a preparation from a single-stranded circular DNA. Examiner has used Moriya to teach a preparation from a single-stranded circular DNA.

Applicant further argues that Moriya does not teach base conversion of a target DNA. Examiner disagrees. See title where targeted base conversion in simian kidney cells is taught. Thus Moriya teaches an in vitro base conversion method of a DNA sequence.

Applicant further argues motivation to combine references. Examiner has provided the motivation to combine and is being reiterated below: It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to practice the method of Zarling et al. in the method of Moriya. The motivation to do so is provided to one of ordinary skill in the art by knowledge of art itself.

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One of ordinary skill in the art knows that based on the size of the target one can clone appropriate size fragment in the multiple cloning site of the chosen phagemid vector.

Further one of ordinary skill in the art knows that shuttle phagemid vectors have architecture that allows one to express the desired (+ also referred as sense strand) or (- also referred as antisense strand). So the desired sense or antisense strand of desired DNA can be produced as single stranded DNA. Moriya teaches how desired fragment can be cleaved from this single stranded DNA. Any single stranded DNA whether linear fragment or single stranded circular DNA can be introduced into the chosen cell to be transfected as taught by Moriya.

One of ordinary skill in the art also has a reasonable expectation that by practicing the method of Zarling et al. in the method of Moriya, i.e. by cloning 300-3,000 bp region of desired target in the phagemid taught by Moriya, one of ordinary skill in the art would be able to prepare desired (either sense or antisense) single stranded DNA fragment. This single stranded DNA fragment obtained can be transfected into desired host cells to successfully perform targeted homologous recombination. See 2144.06 Art Recognized Equivalence for the Same Purpose [R-6]>II. < SUBSTITUTING

#### EQUIVALENTS KNOWN FOR THE SAME PURPOSE

In order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. *In re Fout*, 675 F.2d 297, 213 USPQ 532 (CCPA 1982).

Hence Examiner is maintaining the previously cited rejections over Moriya and Zarling et al.

***Claim Rejections - 35 USC § 103***

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 12-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moriya (1993) Proc. Natl. Acad. Sci. USA vol. 90 pp1122-1126 (previously cited) in view of Zarling et al. (US PG PUB 2004/0019916 A1 with priority back to 1997—previously cited).

Regarding claim 12, Moriya teaches an *in vitro* base conversion method of a DNA sequence (see title where targeted base conversion in simian kidney cells is taught. Thus Moriya teaches an *in vitro* base conversion method of a DNA sequence),

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which is a method of converting one or more bases in a target DNA sequence in a cell, (see page 1124 section neo Transformation of COS ts2 with ss PMS2(8-oxodG). Here neo gene is the target DNA sequence in a COS cell),

consisting of preparing a single-stranded DNA (see page 1123 line 1 where ssPMS2 DNA is taught. Also see page 1122 last par. where isolation of ssPMS2 is taught. Thus by teaching isolation of ssPMS2 DNA, Moriya teaches preparing a single-stranded DNA. See page 1122 right side col. par. 1 where ss shuttle phagemid vector is taught. By teaching ss shuttle phagemid vector, Moriya teaches introduction of single-stranded DNA into the hosts used to shuttle between. Thus teaching introducing a single-stranded DNA)

preparing a single-stranded fragment by cleavage from a single-stranded circular DNA, (see page 1122 Materials and method section where presence of hairpin structure containing *EcoRV* and *Sall* in pMS2 is taught. This hairpin structure containing *EcoRV* and *Sall* is used to linearize ssPMS2. Thus Moriya teaches cleavage of (ssPMS2) a single-stranded circular DNA using restriction enzymes to prepare a fragment)

and introducing single-stranded DNA into a cell (see page 1123 Results section where transfection of COS cells with ss pMS2 is taught. By teaching transfection, Moriya teaches introducing ss DNA fragment into a cell),

wherein said single-stranded DNA is homologous with either a sense strand or an antisense strand of the target DNA sequence, and contains the bases(s) to be converted. (see page 1123 section results where transfection of COS ts2 cells with ss pMS2(dG) is taught. Also see page 1124 section neo transformation of COS ts2 with ss

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pMS2(8-OxodG). These transfections results in production of NeoR colonies. Thus teaching wherein said single-stranded DNA is homologous with either a sense strand or an antisense strand of the target DNA neo gene, and contains the bases(s) to be converted)

Regarding claim 13, Moriya teaches wherein the single-stranded circular DNA is a phagemid DNA (see above as described in claim 12).

Regarding claim 12, Moriya does not teach:

a fragment having 300 to 3,000 bases,

Regarding claim 12, Zarling et al. teaches a fragment having 300 to 3,000 bases (see page 19 par. 0150, where wild type CFTR 491 mer ssDNA fragment is taught. By teaching fragment of 491 mer Zarling et al. teach a fragment having 300 to 3,000 bases) is homologous with the target DNA sequence, and contains the base(s) to be converted (see page 19 par. 0150 where CFTR genomic DNA containing a 3bp  $\Delta$ F508 deletion is taught as the target that is homologous to the Wild type CFTR sequence contained in the 491 mer ss DNA fragment),

wherein the single-stranded DNA fragment is homologous with either a sense strand or an antisense strand of the target DNA (see page 16 par. 0132 where selection of 491 bp region of the CFTR gene spanning exon 11 and containing 3' and 5' flanking intron sequences from published data is described. This 491 bp region from wild type CFTR gene contains both the strands.

Thus based on which strand (+ or – strand ) of the 491 bp is produced as single strand from the phagemid vector taught by Moriya, one will get the single-stranded DNA

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fragment is homologous with either a sense strand or an antisense strand of the target DNA.

Regarding claim 14, Zarling et al. teaches wherein the single-stranded DNA fragment is homologous with a sense strand of the target DNA sequence (see page 16 par. 0133 and 0134 where 491 bp PCR fragment is denatured to produce two single stranded 491 base sequences. Each of the denatured strands are coated with recA protein and introduced into cells. Thus by teaching mixture of both sense and antisense strands Zarling et al. teaches wherein the single-stranded DNA fragment is homologous with a sense strand of the target DNA sequence).

Regarding claim 15, Zarling et al. teaches wherein the target DNA sequence in the cell is a DNA sequence causing a disease due to the one or more bases (see page 16 par. 0131 where target DNA associated with CFTR gene is taught. CFTR is associated with human disease cystic fibrosis. See page 19 par. 0150 where CFTR genomic DNA containing a 3bp  $\Delta$ F508 deletion is taught as the target that causes disease)

Regarding claim 16, Zarling et al. teaches wherein one or more bases in a target DNA sequence in a cell of an organism are converted (see page 18 par. 0147 where homologous recombination between the targeting polynucleotide comprising WT CFTR and  $\Delta$ F508 mutant cellular DNA allelic target in transfected-CF-cells is taught)

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to practice the method of Zarling et al. in the method of



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Moriya. The motivation to do so is provided to one of ordinary skill in the art by knowledge of art itself.

One of ordinary skill in the art knows that based on the size of the target one can clone appropriate size fragment in the multiple cloning site of the chosen phagemid vector.

Further one of ordinary skill in the art knows that shuttle phagemid vectors have architecture that allows one to express the desired (+ also referred as sense strand) or (- also referred as antisense strand). So the desired sense or antisense strand of desired DNA can be produced as single stranded DNA. Moriya teaches how single stranded circular DNA can be cleaved to obtain desired linear single stranded fragment. Single stranded DNA (linear fragment or circular DNA) can be introduced into the chosen cell to be transfected as taught by Moriya.

One of ordinary skill in the art also has a reasonable expectation that by practicing the method of Zarling et al. in the method of Moriya, i.e. by cloning the 300-3,000 bp fragment of desired target from CFTR gene in the phagemid taught by Moriya, one of ordinary skill will be able to make preparations of desired (either sense or antisense) single stranded DNA fragment. This linear single stranded fragment thus obtained can be transfected into desired host cells to successfully perform targeted homologous recombination. See 2144.06 Art Recognized Equivalence for the Same Purpose [R-6]>II. < SUBSTITUTING EQUIVALENTS KNOWN FOR THE SAME PURPOSE

In order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's

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disclosure or the mere fact that the components at issue are functional or mechanical equivalents. An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. *In re Fout*, 675 F.2d 297, 213 USPQ 532 (CCPA 1982).

### ***Conclusion***

6. All claims under consideration 12-16 are rejected over prior art.
7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUCHIRA PANDE whose telephone number is (571)272-9052. The examiner can normally be reached on 8:30 am -5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Examiner  
Art Unit 1637

/Teresa E Strzelecka/  
Primary Examiner, Art Unit 1637  
October 23, 2009